

FILE

L2 ANSWER 1 OF 2 MEDLINE  
AN 94033729 MEDLINE  
DN 94033729  
TI **Particle bombardment:** a universal approach for  
gene transfer to cells and tissues.  
AU **Klein T M;** Fitzpatrick-McElligott S  
CS DuPont Agricultural Products, Experimental Station, Wilmington,  
Delaware 19880..  
SO CURRENT OPINION IN BIOTECHNOLOGY, (1993 Oct) 4 (5) 583-90. Ref: 90  
Journal code: A92. ISSN: 0958-1669.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS B  
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L2 ANSWER 1 OF 2 MEDLINE  
AB In the past year, significant progress in the field of gene transfer  
has been made possible by refinement of the technique of  
**particle bombardment**. The process has been  
utilized for the study of gene expression in plastids and  
mitochondria, the production of transgenic crop plants and gene  
transfer into live animals. Bombarding tissues of live animals with  
genes that code for antigenic proteins may provide an effective  
means of vaccination.

L5 ANSWER 5 OF 8 MEDLINE  
AN 95124254 MEDLINE  
DN 95124254  
TI Gene gun transfection of animal cells and **genetic immunization.**  
AU **Johnston S A**; Tang D C  
CS Department of Internal Medicine, University of Texas Southwestern Medical School, Dallas 75235.  
SO METHODS IN CELL BIOLOGY, (1994) 43 Pt A 353-65. Ref: 27  
Journal code: MV4. ISSN: 0091-679X.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)  
LA English  
FS Priority Journals  
E

L5 ANSWER 5 OF 8 MEDLINE  
AB Gene gun technology at this point has the most utility in animal protein expression as a back-up technology. In other words, when other conventional systems fail, it will generally work. Most notable is its usefulness for hard-to-transfect cells or in some particular in situ applications. Improvements in the gun itself and in the microprojectiles present the potential for this technology to expand in utility. The one area in which it now appears to be the method of choice is **genetic immunization.**

L18 ANSWER 1 OF 2 MEDLINE  
AN 95310070 MEDLINE  
DN 95310070  
TI Mouse embryo fibroblasts transformed by activated ras or dominant-negative **p53** express cross-reactive **tumor rejection antigens**.  
AU Appleman L J; Uyeki J; Frey A B  
CS Department of Cell Biology, New York University Medical Center, NY 10016, USA..  
NC 5T32 GM07308 (NIGMS)  
5T35 DK07421-13 (NIDDK)  
CA 16087 (NCI)  
SO INTERNATIONAL JOURNAL OF CANCER, (1995 Jun 9) 61 (6) 887-94.  
Journal code: GQU. ISSN: 0020-7136.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 199509

L18 ANSWER 1 OF 2 MEDLINE  
AB To study the immune response against oncogene-transformed tumors, C3H/HcN mouse embryo fibroblasts (MEF) were transfected with an activated allele of the H-ras proto-oncogene VaII2 and a dominant-negative allele of the murine **p53** tumor suppressor gene VaII35. Transformed cell lines were derived and found to be tumorigenic in syngeneic mice. Immunization with irradiated **p53** + ras-transformed MEF, but not primary MEF or unrelated syngeneic cells, protected mice from subsequent challenge with live tumor cells. The role of different immune cell subsets in the effector phase of anti-tumor immunity induced by immunization with **p53** + ras-transformed MEF was investigated by in vivo antibody depletion experiments. Immunized mice depleted of CD8+ T, NK or B cells were resistant, but depletion of CD4+ T cells rendered mice susceptible to tumorigenic challenge. In contrast to the tumor-specific immune responses mounted against most chemically or UV-induced tumors, a series of independently derived **p53** + ras-transformed MEF were cross-reactive in tumor rejection assays. In addition, immunization with C3H-derived L-929 cell lines expressing single gene products H-ras or **p53** did not protect mice against tumorigenic challenge with **p53** + ras-transformed tumors. However, MEF transformed by expression of either H-ras or **p53** were cross-protective in vivo. Our data suggest that the **p53** + ras-transformed MEF share **tumor rejection antigens** which are also induced by single gene transformation of the parental primary cell but are not the products of oncogenic ras or **p53** protein.

L18 ANSWER 2 OF 2 MEDLINE  
AN 94007346 MEDLINE  
DN 94007346  
TI Rat adenocarcinoma 13762 expresses **tumor rejection antigens** but **tumor**-bearing animals exhibit tumor-specific immunosuppression.  
AU Frey A B; Appleman L J  
CS Department of Cell Biology, New York University School of Medicine, New York 10016.  
NC CA16087 (NCI)  
SO7 RR5399-27 (NCRR)  
R01CA-57797 (NCI)  
+  
SO CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1993 Nov) 69 (2) 223-33.  
Journal code: DEA. ISSN: 0090-1229.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 199401

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L18 2 AB

L18 ANSWER 2 OF 2 MEDLINE  
AB Rat adenocarcinoma 13762 was adapted to continuous growth in culture and used in a variety of experiments to investigate the immune response to inoculation of animals with replication-defective tumor cells. The results demonstrate that 13762 cells express **tumor-specific tumor rejection antigens** that elicit protective immunity to tumorigenic challenge. By several criteria there is no apparent humoral component of the anti-tumor immunity; however, anti-tumor immunity is characterized by nylon-wool nonadherent spleen T cells. Anti-tumor T cells demonstrate tumoricidal activity in local adoptive transfer assays and are not found in spleens of naive animals or animals immunized against either nontumorigenic Rat 1 cells or a syngeneic fibrosarcoma. Despite the expression of **tumor rejection antigens** 13762 **tumor**, and the demonstrable ability of injection of irradiated tumor to induce anti-tumor immunity, tumors elicited in unimmunized syngeneic animals grow progressively. The reasons for growth of antigenic tumor are unknown but are shown not to be due to defective antigen expression in 13762 tumor since, in addition to being able to elicit T cell immune response in immunized animals, 13762 tumor expresses MHC Class I molecules and can be a target for allogeneic T cell recognition in vitro. These data suggest that in tumor-bearing animals an effective anti-tumor immune response is either not initiated or down-regulated. Since animals bearing 13762 tumors can be immunized against an unrelated syngeneic sarcoma, can produce humoral responses to several protein antigens, and can produce delayed type hypersensitivity response against dinitrofluorobenzene, the immune response to 13762-induced tumors appears specifically suppressed. In support of this contention, 13762 cells express high levels of transforming growth factor beta 1 in vitro which is postulated to impact upon the nascent anti-tumor immune response.

L16 ANSWER 30 OF 30 MEDLINE  
AN 95221901 MEDLINE  
DN 95221901  
TI Recognition of multiple epitopes in the human melanoma  
**antigen** gp100 by **tumor**-infiltrating T lymphocytes  
associated with in vivo tumor regression.  
AU Kawakami Y; Eliyahu S; Jennings C; Sakaguchi K; Kang X; Southwood S;  
Robbins P F; Sette A; Appella E; Rosenberg S A  
CS Surgery Branch, National Cancer Institute, National Institutes of  
Health, Bethesda, MD 20892, USA..  
SO JOURNAL OF IMMUNOLOGY, (1995 Apr 15) 154 (8) 3961-8.  
Journal code: IFB. ISSN: 0022-1767.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals  
EM 199507

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L16 30 AB

L16 ANSWER 30 OF 30 MEDLINE  
AB Four of ten HLA-A2-restricted melanoma specific CTL that were  
derived from tumor-infiltrating lymphocytes (TIL) and administered  
to patients recognized the gp100 melanoma Ag and nine of ten  
recognized the MART-1 Ag. Adoptive transfer of the four  
gp100-reactive CTL, but not the other TIL, resulted in tumor  
regression when infused into autologous patients along with IL-2.  
Tumor regression was thus correlated with the recognition of gp100  
by the administered T cells ( $p = 0.0048$ ). To identify the epitopes  
recognized by these four gp100-reactive CTL, 169 peptides containing  
HLA-A2.1 binding motifs were synthesized and screened for their  
recognition by TIL using cytotoxicity and IFN-gamma release assays.  
Five gp100 epitopes (two for TIL620, three for TIL660, one for  
TIL1143, and two for TIL1200) were recognized by CTL derived from  
different patients. Five of eight HLA-A2 binding melanoma epitopes  
(five gp100, one MART-1/**Melan-A**, two tyrosinase)  
had intermediate binding affinity to HLA-A2.1. These gp100 epitopes  
may be responsible for mediating tumor rejection in vivo and thus  
may be useful for the development of immunotherapies for patients  
with melanoma.

L11 ANSWER 2 OF 2 MEDLINE  
AN 94280772 MEDLINE  
DN 94280772  
TI Tumor antigens recognized by T lymphocytes.  
AU Boon T; Cerottini J C; Van den Eynde B; van der Bruggen P; Van Pel A  
CS Ludwig Institute for Cancer Research, Brussels, Belgium..  
SO ANNUAL REVIEW OF IMMUNOLOGY, (1994) 12 337-65. Ref: 176  
Journal code: ALO. ISSN: 0732-0582.  
CY United States  
DT Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, ACADEMIC)  
LA English  
FS Priority Journals  
E

L11 ANSWER 2 OF 2 MEDLINE  
AB Transplantation experiments have demonstrated that most **mouse** tumors express antigens that can constitute targets for rejection responses mediated by syngeneic T lymphocytes. For human tumors, autologous cultures mixing tumor cells and blood lymphocytes or tumor-infiltrating lymphocytes have produced CD8+ and CD4+ cytolytic T cell (CTL) clones that recognize tumor cells specifically. Attempts to identify the target antigens by biochemical fractionation of tumor cells up to now have failed, with the important exception of the identification of underglycosylated mucins present on breast and pancreatic carcinomas. Gene transfection approaches have proved more successful. A gene family named MAGE codes for antigens recognized by autologous CTL on a melanoma tumor. These genes are not expressed in normal tissues except for testis. They are expressed in many tumors of several histological types. Differentiation antigens coded by genes such as tyrosinase are also recognized on human melanoma by autologous CTL. The identification of human **tumor rejection antigens** opens new possibilities for systematic approaches to the specific immune therapy of cancer.

L21 ANSWER 11 OF 32 MEDLINE

AN 95188447 MEDLINE

DN 95188447

TI **DNA-mediated immunization and the energetic immune response to hepatitis B surface antigen**

AU Whalen R G; Davis H L

CS Department of Molecular Biology, Pasteur Institute, Paris, France..

SO CLINICAL IMMUNOLOGY AND IMMUNOPATHOLOGY, (1995 Apr) 75 (1) 1-12.

Ref: 51

Journal code: DEA. ISSN: 0090-1229.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LA English

FS Priority Journals; Cancer Journals

E

L21 ANSWER 11 OF 32 MEDLINE

AB A new and unusual approach for evoking an immune response has recently been introduced--that of **DNA-based immunization**. Purified plasmid **DNA**, containing protein coding sequences and the necessary regulatory elements to express them, can be introduced into tissues of the organism by means of a parenteral injection or by **particle bombardment**. The number of cells transfected and the amount of protein produced is sufficient to produce a remarkably strong and broad-based immune response to a wide variety of foreign proteins. The absence of an exogenous infectious agent or immunogen results in the abrupt appearance of a foreign protein within the normal cells of an immunologically mature and healthy animal and provokes an energetic and efficient reaction to this form of **antigen** presentation. This review summarizes the results obtained with the various experimental models that have been described to date and considers in greater depth the immune response to the surface **antigen** of the human **hepatitis B** virus that has been achieved using **DNA-based immunization**. Several issues are addressed in a prospective manner in order to anticipate some future developments and to point out topics likely to be pertinent to this field. **DNA-mediated induction** of immune responses may soon be applied as a form of therapeutic treatment. Although this method may constitute a revolution for vaccination, many issues must first be dealt with, especially concerning the safety of using **DNA** as an immunizing molecule.

L5 ANSWER 8 OF 8 MEDLINE  
AN 92186961 MEDLINE  
DN 92186961  
TI **Genetic immunization** is a simple method for  
eliciting an immune response.  
AU Tang D C; DeVit M; **Johnston S A**  
CS Department of Medicine, University of Texas, Dallas 75235-8573..  
SO NATURE, (1992 Mar 12) 356 (6365) 152-4.  
Journal code: NSC. ISSN: 0028-0836.  
CY ENGLAND: United Kingdom  
DT Journal; Article; (JOURNAL ARTICLE)  
LA English  
FS Priority Journals; Cancer Journals  
EM 199206

=> d 15 8 ab

L5 ANSWER 8 OF 8 MEDLINE  
AB To produce an immune reaction against a foreign protein usually  
requires purification of that protein, which is then injected into  
an animal. The isolation of enough pure protein is time-consuming  
and sometimes difficult. Here we report that such a response can  
also be elicited by introducing the gene encoding a protein directly  
into the skin of mice. This is achieved using a hand-held form of  
the biolistic system which can propel DNA-coated gold  
microprojectiles directly into cells in the living animal.  
**Genetic immunization** may be time- and  
labour-saving in producing antibodies and may offer a unique method  
for vaccination.



L5 ANSWER 60 OF 91 MEDLINE

AN 94296659 MEDLINE

DN 94296659

TI Production of monoclonal antibodies by genetic immunization.

AU Barry M A; Barry M E; Johnston S A

CS University of Texas Southwestern Medical Center, Dallas..

SO BIOTECHNIQUES, (1994 Apr) 16 (4) 616-8, 620.

Journal code: AN3. ISSN: 0736-6205.

CY United States

DT Report; (TECHNICAL REPORT)

LA English

FS Priority Journals

E

L5 ANSWER 60 OF 91 MEDLINE

AB Genetic immunization is a simple method for producing polyclonal antibodies in mice. To test if this approach could be used for monoclonal antibody production, **biolistic** transfection was used to immunize a mouse. High levels of polyclonal antibodies against human growth hormone (hGH) were elicited following three inoculations with the gene for hGH. When hybridoma cells were created from the mouse's splenocytes, approximately 17% secreted antibodies vs. hGH. Of these, some recognized only native or denatured hGH, while most recognized both forms of the protein. These findings demonstrate the utility of genetic immunization as method to produce monoclonal antibodies.

L5 ANSWER 61 OF 91 MEDLINE  
 AN 94253560 MEDLINE  
 DN 94253560  
 TI Generation of allo-reactive cytotoxic T lymphocytes by particle bombardment-mediated gene transfer.  
 AU Hui K M; Sabapathy T K; Oei A A; Chia T F  
 CS Laboratory of Molecular Immunology, National University of Singapore..  
 SO JOURNAL OF IMMUNOLOGICAL METHODS, (1994 May 16) 171 (2) 147-55.  
 Journal code: IFE. ISSN: 0022-1759.  
 CY Netherlands  
 DT Journal; Article; (JOURNAL ARTICLE)  
 LA English  
 FS Priority Journals; Cancer Journals  
 E

L5 ANSWER 61 OF 91 MEDLINE  
 AB Mature T lymphocytes comprise functionally distinct subsets with discrete roles in the regulation of the immune response. The cellular basis of the anti-tumor effect is now understood to involve the activation and expansion of tumor-specific cytotoxic T lymphocytes (CTL). To immuno-potentiate the generation of CTL, we have employed the **biolistic** system for the genetic immunization of mice. Here, we report the efficient generation of anti-H-2Kb allo-reactive CTL by particle acceleration-mediated genetic immunization of mouse spleen cells with H-2Kb DNA. The insertion and expression of exogenous gene into host spleen cells following in situ genetic inoculation to effect the generation of a cellular immune response may permit novel alternative strategies for immunotherapy.